meaning of the terms "vaccine" and "to inhibit clinical cancer" as used in the claims on appeal.

Appellants therefore, respectfully request reconsideration of the Board's decision in view of the comments below.

I. Evidence Of Record Overlooked By The Board

In rendering its decision the Board states that the basis of the claimed invention is unsupported by scientific evidence. The Board also states that the prior art of record discloses that no other antibodies to tumor antigens have been demonstrated to successfully prevent or treat cancer.

It is submitted that the prior art of record, i.e., *Cancer Vaccines, Structural Basis for Vaccine Development*, An International Symposium sponsored by Cancer Research Institute, October 3-5, 1994, ("Cancer Vaccines"), which was discussed in Appellant's Appeal Brief and in Appellant's Supplemental Communication filed June 7, 1995, clearly demonstrates that those skilled in the art believed at the time of the invention that antigens present on tumor cells can be exploited as cancer vaccines. The prior art of record also demonstrates that families of tumor antigens are recognized by immune cells such as cytolytic T cells and are exploitable as a means to control cancer. Finally, the prior art of record also discloses that scientists had identified certain antigenic peptides different from the present antigenic peptides that are expressed in a significant proportion of tumors of different histological types, such as melanomas, head and neck carcinomas, non small cell lung carcinoma and bladder tumors that are recognized by cytolytic T cells. Thus, it is respectfully submitted that had the Board considered the prior art of record it could not have concluded that the present invention is not enabled for the reasons asserted. A copy of the prior art is provided for the convenience of the Board.

Cancer Vaccines includes several abstracts of seminars and posters presented by scientists in the field of cancer vaccine research on work that had been in progress at or before the time of the claimed invention. The Abstracts presented at the symposium describe a wide range of tumors and animal systems in which immunity to the tumors was induced using a peptide vaccine based on tumor antigens. These abstracts clearly demonstrate that the skilled practitioner believed at the time of the claimed invention that cancer is treatable or

preventable with cancer specific peptide vaccines and that peptide vaccines can indeed induce immunity to cancer. These abstracts demonstrate that the use of protein vaccines as anti-cancer agents or vaccines was well accepted in the art at the time of the invention (and indeed is still widely accepted by those of skill in the art). Many of the peptide-based vaccines described in the abstracts were at that time being tested in clinical trials, as is clearly stated in several of the abstracts [*See* Abstract S05, last paragraph; Abstract S06; Abstract S22; Abstract S25]. The *in vivo* results from those clinical trials that were reported in the cited Abstracts bear out the results obtained from *in vitro* studies concerning the cytotxicity of antibodies that are specific to the peptide vaccines.

Abstract S14 of *Cancer Vaccines* includes data obtained with tumor-derived peptides that demonstrate that the peptide vaccines provide protective immunity in animal models. ["Vaccinating syngenic animals with either of the synthetic peptides protected them against the generation of metastasis and resulted in long-term survival."] [last paragraph] Thus, the prior art of record establishes that

(1) those skilled in the art at the time of the invention believed that cancer can be treated and/or prevented effectively by vaccinating individuals with antigenic peptides based on tumor peptides; (2) demonstrated that several different tumor-based peptide vaccines were in clinical trials; and (3) provided a correlation between the *in vitro* observed cytotoxicity of T cells having immunological specificity to the tumor peptides and effective treatment of cancer using the anticancer peptides *in vivo*.

Furthermore, as discussed in several of the abstracts from the *Cancer Vaccines Symposium*, several research laboratories were actively testing peptide families that were demonstrated to be expressed in several different histological types of tumors. [*See* Abstract S03, Thierry Boon et al.; "MAGE, BAGE and GAGE [three different antigenic peptides found to be expressed only in tumor cells] are expressed in a significant proportion of tumors of different histological types such as melanomas, head and neck carcinomas, non small cell lung carcinoma and bladder tumors."]. These authors also disclosed that these antigens were recognized on human melanomas by autologous cytolytic T cells (CTL). Thus, the prior art of record demonstrated that antigenic peptides that are present on a wide variety of different histological types of tumors exist and **are recognized by cytolytic T cells**. Recognition by cytolytic T cells, i.e., binding of CTL to a cell, is known in the art to directly correlate with

killing of the recognized cell or otherwise prevention of cell division.

The results reported in these various Abstracts from the *Cancer Vaccine Symposium* provide strong evidence of the enablement of the claimed invention. The peptide vaccine of the claimed invention differs from those reported at the Symposium in that a different, heretofore unknown tumor antigen is used to confer immunity or treatment of cancer in the present invention.

It is respectfully submitted that had this prior art of record been considered by the Board it could not have concluded that there is no correlation between the *in vitro* data and *in vivo* results observed with the claimed tumor antigen peptide; could not have concluded that the prior art discloses no tumor antigen specific antibodies that are effective *in vivo* as vaccines for treating or preventing cancer; and could not have concluded that the claimed invention is not enabled.

II. Misapprehension Of Claim Terms

The Board stated that claim 1 is drawn to a method comprising administering a vaccine, while claim 2 is directed to a vaccine product. The Board then construed the term "vaccine" as used in these claims without giving any consideration to claim language that directly defined the functionality of the "vaccine." That is, the Board determined that the term "vaccine" as used throughout the specification and claims must have the art-accepted meaning and therefore, the claims must be construed to encompass a product and method that protects the vaccinated patient from developing clinical cancer.

It is respectfully submitted that the claim language was misconstrued since other functional language set forth in the claims was disregarded or misapprehended.

Appellant agrees with the Board that the claims are directed to a method of administering a "vaccine" and a "vaccine product." However, contrary to the Board's assertion otherwise, the claims, as well as the specification, provide an explanation as to what is meant by the term "vaccine." Claim 1 includes the limitation that the claimed process is a process for "inhibiting or destroying cancer cells, to prevent the development of clinical cancer, **or if it has already developed, to inhibit or destroy clinical cancer**." According to claim 2, the "vaccine product" upon administration to a patient "will cause cancer cells . . . to be inhibited or destroyed and will prevent the development of clinical cancer, **or if it has**

already developed, will destroy the cancer cells or inhibit their growth." Thus, the term "vaccine" is used and defined differently in these claims than is used by the Board.

The term as applied by the Board is limited to a prophylaxic measure or composition, i.e., will prevent the development of a specified disease. The art-accepted term does not normally include compositions used to treat disease that is already present. For example, the measles vaccine or hepatitis vaccine is not given to patients who present with measles or hepatitis. Instead, the vaccine is given before any clinical symptoms of the disease appear and must be given long enough in advance of the patient contracting the disease to be effective as a vaccine. If given after disease symptoms develop, the vaccine is ineffective.

In contrast, the present invention is directed to a method and composition that can be administered even after clinical symptoms of disease have occurred. As such, the claimed "vaccine" as defined in the claims and at pages 17 through 18 (Example 8) of the specification is different from the art-accepted term. Thus, the Board erred in narrowly construing the claims to require that the method and composition prevent development of cancer and then finding lack of enablement because Appellant had not sufficiently demonstrated such prevention.

The claimed method and composition are properly construed to include those methods and compositions, respectively, which inhibit the growth of cancer cells. Appellant's data that are set forth in the specification and the data discussed in the prior art of record discussed above, clearly demonstrate that the claimed peptide vaccine induces production and release of cytolytic T cells that recognize cancer cells. It is well known in the art that binding of T cells to an antigen on a cell results in lysis of the cell. CTLs kill only those cells to which they attach and bystander cells are not injured. A CTL is activated by cross-linking of its antigen receptor. Binding of a CTL to a target cell is known in the art to be sufficient to lyse the target cell. That is why the authors of Abstract S03 (Boon et al.) of *Clinical Vaccines* report that they had "isolated a number of genes that code for antigens recognized on human melanomas by autologous cytolytic T cells (CTL)." If the CTLs merely bound to the cancer cells, but had no further effect, there would have been no point to the disclosed research, which is entitled "Genes Coding For Tumor Rejection Antigens." Clearly, these researchers in the field of cancer vaccines understand CTL recognition of cancer cells to be more than mere binding, understanding it to mean "tumor rejection", e.g., tumor cell death or inhibition.